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10/057,810	01/24/2002	Xianqiang Li	26757-709	4240

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,810	LI ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31 and 47-50* is/are pending in the application.

4a) Of the above claim(s) *25-28 and 47-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I, claims 1-31 and the following species: 1) at least 10 different cis elements (claim 2); 2) at least 2 copies of the cis element (claim 6), 3) cis element having a length of 5-100 base pairs (claim 9); 4) the variable sequence of the reporter sequence being at least 15 bases in length (claim 5); 5) Hela cell line as a species of the mammalian cell line (claim 18), 6) at least 10 different reporter sequences (claim 21), 7) 5' priming sequence, the whole or a part of which is included in or a complement of the reporter sequences listed Figure 2 under the column labeled as Reporter Sequence, (claim 25), 8) 3' priming sequence, the whole or a part of which is included in or a complement of the reporter sequences listed Figure 2 under the column labeled as Reporter Sequence (claim25); 9) a library of hybridization probes that hybridize to the reporter sequences listed Figure 2 under the column labeled as Reporter Sequence or to the complements thereof (claim 27); 10) a reporter protein that can be expressed by the cell as disclosed in the Specification on page 18, lines 22-26 (claim 29), 11) a library of antibodies that are selective for the expressed protein as

disclosed in the specification on page 14, lines 23-24 (claim 30) is acknowledged.

Upon reconsideration of the species restriction with respect to the number of cis and reporter elements, the species is withdrawn.

Claims 25-28 and 47-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement. [Note that claims 47-50 are withdrawn since these claims relate to the identifying of the type of the cell sample which will encompass different process step].

Status of Claims

Claims 1-31 and 47-50 are pending in the application.

Claims 32-46 have been cancelled.

Claims 25-28 and 47-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1-24 and 29-31 are under examination.

Specification

The abstract of the disclosure is objected to because it is too long. Also, because of the use of phraseology often found in

patent claims e.g., "comprises". Correction is required. See MPEP § 608.01(b).

Applicants are reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1-24 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to teach how to make and use the instantly claimed method of identifying multiple activated transcription factor with any cis element, promoter and reporter sequences. Also, the description of the specification is not adequate to describe the claimed scope of the invention. The specification at Figure 2 provides a list of the different cis element with the corresponding transcription factor and reporter sequence. It is not apparent from the listing the relative amount

or combinations of the kind of the different cis and/or reporters comprise in the library. It cannot be ascertained whether the library formed from the different cis elements/reporter sequences results in a true representation of the different listed cis elements to enable identifying a transcription factors present in a sample. The teachings in the specification are all general teachings relating without guidance as to the picking of the individual components that can be employed in the method. Likewise, there is no process step as to a library wherein the recognition sequence and/or cis contained therein is varied or to the library of hybridization probes used in the hybridization assay in the determination of the different varied reporter. Furthermore, the specification fails to identify a single activated transcription factor that forms a complex with the cis/reporter, let alone, the innumerable activated tf present in a biological sample. Neither was there a single biological sample given to show that even a single activated tf has been identified. More so for the numerous different unknown activated transcription factors that has been identified. This is made more compelling because not a single working example has been

provided. There are no specific experimental conditions that are described to identify the numerous tfs present in a complex cell sample. Thus, there is no direction or guidance for a skilled artisan as to the practice of the claimed invention. As stated by Li et al (US 2002/01686400) at page 8, [0107] ".. it is important to understand that in any library system encoded by oligonucleotide synthesis one cannot have complete control over the codons that will eventually be incorporated into the peptide structure. This is especially true in the case of codons encoding stop signs…" Due to the high level of DNA binding specificity of transcription factors, each transcription factor will typically bind to a different DNA sequence. In some instances, a related family of transcription factors may bind to the same DNA sequence. Selection of the sequences used in the hybridization probes may be based on the different tfs that one wishes to detect in a sample. This in turn may depend on the type of organism, cell, or disease state one wished to identify and/or monitor the gene expression of. The expedient statements in the specification do not relate to an adequate disclosure or to the how to make and use of the claimed invention.

The specification fails to teach how to use and making a library of cells that comprises 100 different cis elements and/or a reporter sequence with 2000 bases in length. See University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 and 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the method of identifying the multiple different activated transcription factors from the cell sample. There appear to be a lack of nexus in the process steps. For example, as to the step of forming mRNA transcription products and the determining step of the reporter sequence comprised in the mRNA transcription products.

The term "more" is a relative term which renders the claim indefinite. The term "more" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. [It is suggested to use ---at least----.]

2. Claim 20 is indefinite as to the "look-up" table, absent such description in the specification.

3. The limitation of the method step in claim 29 is confusing. Claim 1 does not recite for an expression of a reporter protein or a reporter sequences encoding reporter proteins expressed from the mRNA transcription products.

4. "Compliments" is misspelled in claims 24, 26, 27.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-24 and 29-31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,696,256 ('256 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '256 patent encompasses the instant claimed method. The '256 patent recites the specific transcription factor probes that contain the known cis/reporter elements of the instant invention. The '256 Patent and the instant application are drawn to the same method of identifying multiple different tfs in a cell sample using the same components therein i.e. a transcription factor that includes a cis element and reporter sequence. This is especially true since all the applications recite the same known transcription factors, the cis elements contained in the known tf and reporter sequence. Thus, a determination of the known tf in a library, in essence will be a determination of the binding cis fragment contained in said tf.

Claims 1-24 and 29-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 34-49 of

copending application No. 09/947,274('274 application) or over copending application S.N. 09/877,705 ('705 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the copending applications ('274 and '705) is an obvious variant of the instant application. All of the copending applications recite similar process steps of identifying a tf in a cell sample. Each of the applications recites for different components to use in the identifying the tfs in the cell sample. However, all of the disclosures of the copending applications recite the same transcription factor probes or cis element of the transcription factor or modulators of the transcription factor binding. Each of the applications does not provide any Examples for the different components from the same compounds to determine the tfs in the cell sample.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim Rejections - 35 USC § 103

Claims 1-24 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb (6,579,675)

in view of Mauro et al (WO 01/55371) and Kauffman et al (6,413, 723).

Kamb et al discloses at col. 3, lines 5-57 a method of identifying proteins (activated transcription factors as claimed) in a cell sample comprising introducing an expression library of perturbagens comprising e.g., of fragmented gDNA, random cDNA or synthetic DNA of random sequences engineered to contain a reporter gene under the control of a cell type specific cis regulatory sequence,(col. 12, lines 17-26) into the cells. The cells exhibiting changes in reporter expression level are selected. Expression library inserts from the selected cells are isolated, thereby providing a sub-library enriched for sequences that affect the phenotype reflected by the reporter. Further rounds of sub-library introduction and cell selection may be carried out to provide additional enrichment. Sequences

identified using this method may be used to ascertain the identity of additional molecules involved in generating the cellular phenotype. Kamb discloses that the reporter gene is under the control of a specific cis regulatory element. Sequences are isolated from the expression library based on their ability to alter the activity of the cis regulatory sequence, as read out by the reporter expression level. Kamb at col. 8, line 41 up to col. 10 discloses the different reporter genes, e.g., a labeled antibody specifically. Kamb describes the different cis-regulatory element including mutants thereof (variants, as claimed). See further Example 2, col. 20 which specifically discloses the specific components of the process and identification of the transcription factor MITF. However, Kamb does not positively disclose identifying transcription factors in a cell as claimed. However, Mauro et al discloses a method of identifying a transcription factor in a sample by introducing into the cell sample a random library constructs comprising of a promoter with a cis element and a plurality of reporter sequences. The cell sample use is a mammalian cell (e.g., page 7, line 30 up to page 8, line 1). The promoter sequence which contains the cis element and the reporter sequence and the relative positioning of these elements are shown in Fig. 1. The method further comprises determining the

cis elements of the promoter which then reacts with the transcription factor present in the sample. (See e.g., Example 1 at page 47, line 25 up to page 65, line 9, specially page 50).

Kauffman basically discloses the same cis elements as used for identifying tfs as Mauro. Kauffman further discloses that the population of nucleic acids of low diversity can contain, for example, 2, 3, 4, 5, 6, 7, 8, 9, between about 10 and 20, between about 21 and 80, or between about 81 and 200 different nucleic acid molecules. As an example, a population that includes all possible molecules of between 5 and 20 nucleotides in length, including each of the four naturally occurring nucleotides at each position. Such a population of about 10, 20 different nucleic acid molecules inherently includes all possible cis acting nucleic acid elements of up to about 20 nucleotides in length.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine the presence of multiple tfs in the method of Kamb using cis regulatory elements. Mauro or Kauffman positively discloses that cis-elements are the ones that bind and can identify transcription factors in a sample. Furthermore, while Kamb called the proteins binding to cis perturbagens instead of transcription factors however, this might very well be

transcription factors, as identified by Kamb as described in Example 2. The modification i.e., determining the presence of tfs in a sample are expressly articulated by Kamb alone or in combination with Mauro. It is well settled that there is no requirement for motivation, if the modifications are expressly articulated by the combined teachings of the prior at.

Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb in view of Mauro as applied to claims 1, 6, 12, 18-19, 24 and 29 above, and further in view of Weismann et al (6,066,452)

Kamb is discussed supra. Kamb suggests using antibody to detect the reporter proteins but not in an array or in a library. However, Weismann discloses that the binding site can be used to select antibody expressing phages. A crude nuclear extract or a complex of a long DNA probe with multiple binding proteins attached may be used to enrich phage expressing antibodies or portions of antibodies. The complexes may be immobilized, for example on a plastic surface. Weismann further discloses the use of array for the binding elements. Accordingly, it would have been obvious to make a library or an array of antibodies in the method of Kamb since Weismann discloses that said antibody array determination of reporter sequences have been employed in the art. One would have been

motivated to use an array for high throughput screening when a multitude of compounds are present in a sample. The use of array provides for rapid determination of unknown biological interactions, therefore identification of an unknown gene thereby facilitating identification of a potential or candidate therapeutic or diagnostic drugs.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
March 22, 2004